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Trends In Hpv 16/18-Associated Cervical Lesions In New Haven County, Connecticut, 2008-2014

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By

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ABSTRACT

Background: Current vaccines protect against human papillomavirus (HPV) types 16 and 18, which are associated with approximately 70% of cervical cancer and 50% of high-grade cervical lesions. Monitoring trends in HPV 16/18-associated lesions is important to assess vaccine impact.

Methods: Cervical intraepithelial neoplasia (CIN) grades 2 and 3 and adenocarcinoma in situ (AIS) cases of women residing in the catchment area of New Haven County, CT were reported to the Connecticut HPV-IMPACT surveillance system, and diagnostic specimens were obtained for HPV DNA testing. Cases were geocoded to census tracts and linked to area-based measures of race, ethnicity, and poverty. Statistical analysis included logistic regression modeling and generalized estimating equations. This analysis included 1,820 New Haven County women aged 21-39 years diagnosed with CIN2+ from 2008-2014 who had at least one of the fifteen high-risk HPV types detected in the diagnostic specimen.

Results: A total of 825 (45.3%) cases had HPV 16 or 18. Declines in prevalence of HPV 16/18 in lesions were observed, and in a model controlling for age and diagnosis grade, the year 2012 was associated with a lower likelihood of HPV 16/18 compared to the year 2008 (p=0.004). There was a significant interaction between year and area-based race with less of a decline in women living in areas with higher proportion of black residents (p=0.028). Among 21-24 year old women (n=552), there was a more evident decline in likelihood of HPV 16/18 in the lesions controlling for diagnosis grade, but the decline did not occur for women in areas of higher proportions of black, Hispanic, and poor residents.

Conclusion: These results suggest that the proportion of lesions attributed to HPV 16/18 have declined in New Haven County, CT, particularly among young women, but the declines are not observed in areas of higher minorities and higher area-poverty.

Acknowledgements

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Background

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States [1]. The overall prevalence of infection has been estimated at 27% among US women aged 14-59 years, with the highest prevalence of infection among females ages 20-24 [2]. Infection with HPV can cause genital warts as well as high-grade cervical lesions that are known precursors of invasive cervical carcinoma, and HPV infection is recognized as a necessary cause of cervical cancer [3, 4]. Despite declines in cervical cancer incidence and mortality due to screening, 12,000 women in the US were diagnosed with cervical cancer in 2012 [5]. HPV types found in cervical cells have been classified as low or high risk of progression to malignancy based on their epidemiological association with invasive cervical cancer [6]. HPV types 16 and 18 are associated with approximately 70% of cervical cancer worldwide [7]. In addition to types 16 and 18, types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 are considered high-risk types [6]. High-grade cervical lesions, including cervical intraepithelial neoplasia (CIN) grades 2 and 3 and adenocarcinoma in situ (AIS), are important outcomes in monitoring of HPV trends because they are considered precancerous and closely related to the development of cervical cancer, with CIN grade 3 and AIS being the most immediate precursors to invasive cervical cancer [8].

Three highly efficacious prophylactic HPV vaccines that protect against HPV types 16 and 18 have been licensed by the US Food and Drug Administration since 2006 [9, 10]. All three are recommended for routine use among adolescents [9, 10]. The quadrivalent HPV vaccine has been predominantly used in the US since its licensure in 2006, which protects against the low-risk HPV types 6 and 11 that are associated with genital warts, in addition to types 16 and 18 [9]. The newest vaccine was licensed in 2014 and is a 9-valent vaccine that protects against five additional high-risk types: 31, 33, 45, 52, and 58 [10]. As it takes decades for cervical cancer to develop, monitoring of other HPV-associated clinical outcomes is important to demonstrate population-level impact of vaccination. Studies from worldwide data sources to demonstrate the impact of these HPV vaccines show promising results in

consistent and significant declines in HPV-related clinical outcomes among young women, including genital warts and HPV infection [11, 12]. From 2008 to 2012, prevalence of HPV types 16 and 18 in CIN2+ lesions statistically significantly decreased among women in the US who received at least one dose of the vaccine across of five catchment areas in California, Connecticut, New York, Oregon, and Tennessee [13].

An important aspect in monitoring HPV vaccine impact is observing differences or disparities by race, ethnicity, and socioeconomic status. In Connecticut, disparities have been shown in rates of high-grade cervical lesions, and women living in areas of higher levels of poverty and higher proportions of black residents had higher rates of CIN2+ lesions in the early vaccine era of 2008 and 2009 [14]. Black race, Hispanic ethnicity, and higher area-based poverty were all found to be associated with a lower likelihood of HPV 16 and 18 among women in Connecticut with high-grade cervical lesions in 2008 to 2010, which suggests that HPV vaccines could potentially have a lower impact among black and Hispanic women and those living in high poverty areas [15]. It has also been shown that there is an interaction between individual race and ethnicity and area-based measures of race being associated with higher rates of high-grade cervical lesions in Connecticut in 2008 to 2011 [16].

The goal of this analysis is to explore the trends in HPV 16/18-associated high-grade cervical lesions over time in New Haven County, Connecticut from 2008-2014, and to examine trends by individual and area-based measures of race, ethnicity, and poverty to observe potential disparities.

Methods

Design, Case Ascertainment, and Definitions

Surveillance methods have been described previously [14, 17]. The Centers for Disease Control and Prevention (CDC) established the HPV-IMPACT surveillance system in 2008 in collaboration with the Emerging Infections Program (EIP) Network to monitor the impact of HPV vaccination through

population-based surveillance of high-grade cervical lesions [18]. At the Connecticut (CT) site, diagnoses of high-grade cervical lesions, specifically cervical intraepithelial neoplasia (CIN) grades 2 and 3 and adenocarcinoma in situ (AIS), were added to the list of statewide mandatory reportable diseases in 2008 by the Connecticut Department of Public Health [19]. All 34 surgical pathology laboratories in the state are currently in compliance with this reporting requirement. Reports include diagnostic information as well as patient demographics. Standardized reports and samples of diagnostic histopathology specimens of CIN2+ and AIS cases of women aged 18-39 years residing in the catchment area of New Haven County, CT are sent to the CDC for HPV DNA testing [18]. Enhanced surveillance activities for cases residing in New Haven County include medical chart reviews and patient interviews to collect additional demographic and health history information. According to 2010 US Census data, New Haven County has a total population of 862,474, including 13% black and 15% Hispanic residents. The US Census 2006-2010 American Community Survey estimates that 11% of the individuals in New Haven County live below the federal poverty level. There are 189 census tracts in New Haven County, CT.

We analyzed data from cases reported during January 1, 2008 through December 31, 2014 in the catchment area of New Haven County, CT and for whom HPV typing results had been received from the CDC. Cases aged 21-39 and with at least one of the fifteen types of HPV that are considered high-risk detected in the diagnostic specimen were include in this analysis. Presence of HPV 16/18 was defined as detection of either type in a lesion, irrespective of presence of other types. Diagnoses are reported as CIN2, CIN3, CIN2/3 (grade not specified), AIS only, or AIS + CIN. In order to reflect the high-grade lesions that are more immediate precursors to invasive cervical cancer, and due to the small sample size of women diagnosed with AIS, cases were classified for this analysis into one of two diagnosis categories: CIN2 and CIN2/3, and CIN3 and AIS with or without CIN. Individual race and ethnicity measures obtained from surveillance reports were combined to form a single race/ethnicity variable with four categories: non-Hispanic white, Hispanic, non-Hispanic black, and other race or unknown. Insurance information

from reports was classified into broader categories of private, public insurance or no insurance, and other/missing. The cases were grouped into four categories based on age at the time the lesion was detected: 21-24, 25-29, 30-34, and 35-39 years.

Geocoding and Geographic Measures

Cases were geocoded to the census tract level using residential addresses, a method that has been previously described [14, 16]. Census tracts are small subdivisions of counties that are relatively homogenous in population characteristics, and therefore can be used as proxies for neighborhoods [20]. Using geocoded surveillance data and geographic sociodemographic measures from US census data has been shown to be appropriate to examine health disparities [20-22]. Cases were then linked to census tract-level measures of race, ethnicity, and poverty. Area measures of race and ethnicity were obtained from 2010 US Census data and included percentage of the female population that are black and Hispanic, respectively. The percentage of the female population living below the federal poverty level at the census tract level is obtained from the US Census 2006-2010 American Community Survey 5-year estimates. These area-based measures were examined in binary categories (≥20% and <20%), which are adapted from the cut-points used in the Public Health Disparities Geocoding Project, with the three lower levels collapsed into one category for analysis purposes [20].

Statistical analyses

The primary outcome for analysis was presence of HPV 16/18 DNA detected in the diagnostic specimen. To first determine associations with the proportion of high-grade cervical lesions with HPV 16/18, a Chi-square test was used for each variable. Binary logistic regression modeling was then conducted for each individual-level variable (year, age group, diagnosis, race/ethnicity, and insurance), using indicator variables in the model for any variables that had more than two categories, to determine

unadjusted associations with the prevalence of HPV 16/18. For the area-based measure variables, generalized estimating equations were used and the census tract variable was included in the model to account for the correlation between women residing in the same census tract.

To examine the adjusted effect of year, the predictor of interest, on the proportion of HPV 16/18-associated lesions, diagnosis grade and age group were included in the model to adjust for potential confounding. Diagnosis is controlled for because more immediate precursors of cervical cancer (CIN3 and AIS) are more likely to have HPV 16/18.

A series of models were run to assess the interaction between year and the various individual and area-based measures. A model was run for each individual and area-based sociodemographic variable (race/ethnicity, insurance, area race, area ethnicity, and area poverty) to determine significance of the independent effects of the variable and the interaction between year and the variable of interest. All of these models included diagnosis and age to control for potential confounding.

Chi-square tests were used to evaluate associations between year and presence of HPV 16/18 in lesions, stratified by age group. The modeling analyses were then repeated, restricting the sample to the 21-24 year old age group. For purposes of this analysis, years were combined into three categories to mediate the effects of a smaller sample size: 2008-2009, 2010-2011, and 2012-2014. As with the previous set of models, a series of models were run to test the significance of each variable and its interaction with year in this subset of the sample.

All statistical analyses were conducted using SAS version 9.4. Significance was determined at the $\alpha=0.05$ level unless otherwise indicated.

Results

From 2008 to 2014, a total of 2,106 New Haven County women aged 21 to 39 years were diagnosed with CIN2+, reported to the Connecticut HPV-IMPACT surveillance system, and had HPV

typing completed. Of these, 1,842 (87.5%) had at least one of the fifteen high-risk HPV types detected in the diagnostic specimen. We successfully geocoded 1,820 (98.8%) of cases.

A total of 825 (45.3%) cases in the sample had either HPV type 16 or 18 detected in the lesion, including 743 (40.8%) women with HPV 16 only, 92 (5.1%) with HPV 18 only, and 10 (0.6%) with both HPV 16 and 18 detected (Figure 1, Table 1). The other high-risk types most frequently detected in this sample were HPV type 31 (13.9%) and HPV 52 (11.1%), and 11.8% of cases have 2 of more HPV high-risk types detected in diagnostic specimens (Figure 1). Moderate declines were observed in the prevalence of HPV 16/18 in lesions over time during 2008-2014, with the most evident decline observed in the 21-24 year old age group in the sample (Figure 2).

In the unadjusted main effects analysis, black women were significantly less likely to have HPV 16/18 compared to white women in the sample (prevalence ratio [PR]: 0.60, 95% confidence interval [CI]: 0.45, 0.80, Table 2). The main predictor of interest, year, indicates a decrease in the likelihood of HPV 16/18 in lesions for every year compared to 2008, though the only year that was significant was 2012 (p=0.008, Table 2). When adjusting for the effects of age and diagnosis type, women in 2012 were 61% as likely to have HPV 16/18 as women in 2008 (p=0.004, Table 3). In this adjusted analysis, the years 2013 and 2014 are marginally significant at the α=0.10 significance level (adjusted PR=0.69, p=0.097 and adjusted PR=0.64, p=0.093 respectively).

To determine the effects of individual and area-based measures on the prevalence of HPV 16/18 over time, a series of multivariate models adjusting for potential confounding by age and diagnosis were conducted, with interaction terms to determine if there was an interaction between year and the specific measure of interest. There was a significant interaction between year and area-based race (p=0.028), controlling for age and diagnosis. Women in areas with ≥20% of black residents did not show a decline over time in the prevalence of HPV 16/18 compared to women living in areas with <20% of black residents (Figure 3). There was no significant interaction between year and individual

race/ethnicity, insurance status, area-based ethnicity, or area-based poverty (p=0.241, p=0.345, p=0.254, p=0.154, respectively).

A post-hoc analysis of only the women in the sample aged 21-24 years old was completed. Age group was determined to be an effect modifier of the relationship between the main effect of interest, year, and the prevalence of HPV 16/18- associated lesions through stratification of the sample by age group. There is a significant association between year and prevalence of HPV 16/18 in the 21-24 year old age group (Chi-square, p=0.004), but not in the 25-29, 30-34, or 35-39 year age groups (Chi-square, p=0.303, p=0.599, p=0.615, respectively).

For this post-hoc analysis we restricted analyses to the women ages 21-24 (n=522) where there was the most evident decline in the proportion of lesions attributed to HPV 16/18 (Figure 2). As a consequence of the smaller sample size, years were combined into 2008-2009, 2010-2011, and 2012-2014 to examine the changes in the proportion of lesions attributable to HPV 16/18 over time. In an unadjusted analysis among women aged 21-24, cases living in areas with ≥20% of residents of Hispanic ethnicity were significantly more likely to have HPV 16/18-associated lesions (PR: 1.42, 95% CI: 1.01, 2.00, Table 4). Adjusting for diagnosis type, women of age 21-24 with a high-grade lesion diagnosed in the years 2012-2014 were 61% less likely to have HPV 16/18 than women in 2008-2009 (95% CI: 0.40, 0.63, p<0.001, Table 5).

In a series of multivariate models for these 21-24 year old women adjusting for potential confounding by diagnosis, there were significant interactions between year and area-based race, ethnicity, and poverty (p=0.038, p=0.013, and p=0.005, respectively). Young women from areas with <20% of black residents, <20% Hispanic residents, and <20% residents living in poverty showed declines in the prevalence of HPV 16/18 by the years 2012-2014. Young women from areas with ≥20% of black residents did not show as significant a decline in the prevalence of HPV 16/18 compared to the women living in areas with <20% of black residents, and the women from areas with ≥20% of Hispanic residents

or ≥20% of residents living in poverty showed no decrease in prevalence of HPV 16/18 over time (Figure 4). There was no significant interaction between year and individual race/ethnicity or insurance status among these women (p=0.578, p=0.790, respectively).

Discussion

Analyzing the distribution of HPV types 16 and 18 in high-grade lesions is important to assess vaccine impact. In addition, analyzing this distribution by race, ethnicity, and sociodemographic factors is important for determining if the vaccine impact is different among specific populations. This analysis expands our current knowledge about disparities in HPV 16/18 prevalence by individual and area-based measures by examining the changes over time.

In this analysis we observed declines in the proportion of lesions with a high-risk type of HPV that have HPV 16/18 from 2008-2014. This relationship over time significantly interacts with area race, and declines are less evident in women who live in areas with a higher proportion of black residents. Among young women in the sample aged 21-24, the decline in the prevalence of HPV 16/18 in these high-grade lesions differs by area race, area ethnicity, and area poverty. The decline is observed for women in areas of lower proportions of black, Hispanic, and poor residents, but not among the women in areas of higher minorities and a higher proportion of residents living below the poverty level. These findings are consistent with previous declines in high-grade cervical lesions observed in young women in Connecticut from 2008-2011, where significant declining trends occurred in census tracts with lower proportions of the population being black, Hispanic, or living in poverty [17]. Our analysis extends these previous trend analyses by examining the specific HPV vaccine types 16/18 and over a longer period of time.

In these data, the overall trend of proportion of lesions with HPV 16/18 is a moderate decline over time, but upon further exploration of the effect of age on this trend, the overall decline is subdued

by the women of older ages in the sample. The decline in the proportion of lesions with HPV 16/18 is more evident in those women ages 21-24, which is to be expected as these women are more likely to be vaccinated and more likely to be impacted by vaccination. Increasing vaccination rates among young women is a possible explanation for the decline in prevalence of HPV 16/18 in lesions observed here. An important consideration in the interpretation of these findings however is that we can only assess indirect vaccine impact.

This study has some limitations. Women could only be included in this analysis if the HPV DNA testing results had been completed at CDC. This resulted in a smaller number of samples in the later years of our trend analysis, as recent specimens were pending specimen processing at the CDC and typing results were not yet completed or received. While this presents a potential sample size issue, particularly in using a subset of the data for analysis, it is not likely that the typing results received or not yet received in the more recent years presented bias in the results. Another potential limitation is missing demographic information for some cases, particularly for individual-level race and ethnicity for which was missing in 28% of cases in the analysis. For many of the variables used in the analysis, categories had to be created and combined in order to prevent having levels of variables that were too small to be interpreted, such as more detailed individual race or ethnicity, insurance type, or diagnosis type categories. Without an ability to measure trends in the general population, we have used the proportion of high-grade lesions that detect HPV 16/18 to assess trends over time. Changes in cervical cancer screening guidelines that recommend less frequent screening is a possible explanation for declines in the rates of high-grade cervical lesions, but by examining the prevalence of these types among lesions that were reported we should be avoiding any bias as a result of this.

A strength of this analysis is the use of population-based surveillance data with HPV-type specific results. Using high-grade lesions that are reportable to the state of Connecticut gives us confidence that we have high case ascertainment for women living in the catchment area of New Haven

County. The use of geocoded data allows us to assess disparities at the area-based level in addition to individual factors. These findings suggest that monitoring specific HPV types by both individual and area-based measures of race, ethnicity, and poverty is important. Future research is needed to better understand these results and what is driving these disparities. Some possible explanations to explore include different patterns in vaccine uptake, such as timing of vaccination relative to initiation of sexual activity or initiation of vaccination compared to completion of the three-dose series. Differential distributions of HPV types among populations and differences in screening patterns are additional considerations in the interpretation of these findings and how these disparities can best be addressed in practice. Further, additional research can determine if these vaccine-types continue to persist in areas of higher minorities and higher levels of poverty, and how the future impact of HPV vaccines will affect these disparities.

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Figure 1. High-Risk Human Papillomavirus (HPV) Type Prevalence in CIN 2+ Cases Among Women Aged 21-39 Years in New Haven County, Connecticut During 2008-2014 (n=1,820). Presence of types is not mutually exclusive, and more than one HPV high-risk type can be detected in diagnostic samples.

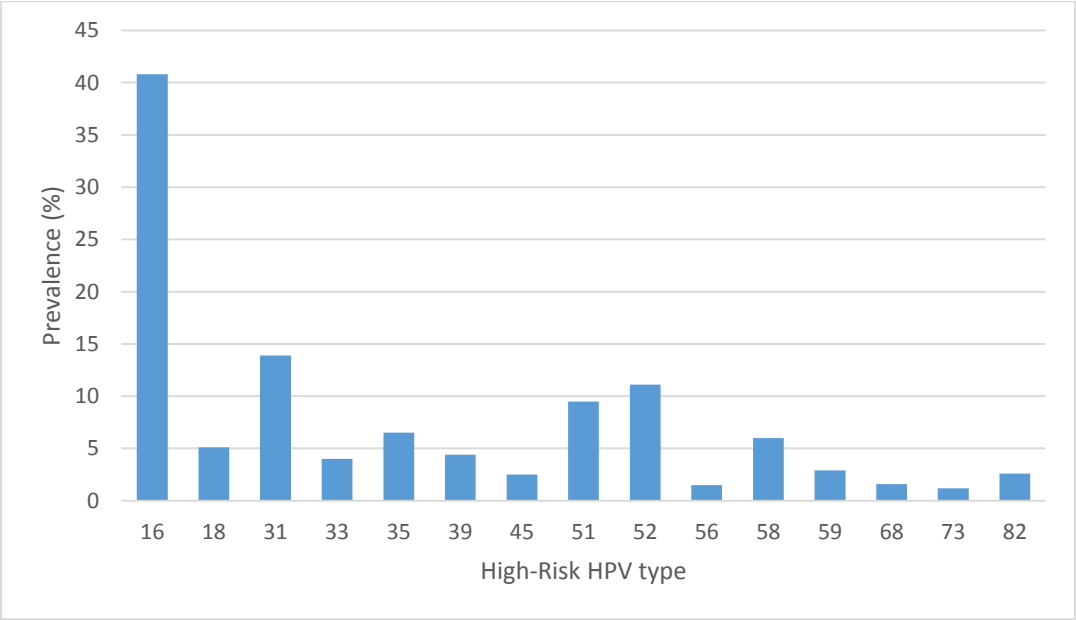

Table 1. Characteristics of CIN2+ Cases with High-Risk HPV Types Among Women Aged 21-39 Years in New Haven County, Connecticut During 2008-2014 (n=1,820)

	Total Number (%)	HPV 16/18 (n=825)	Other High Risk (n=995)	p[a]
Year				0.150
2008	400 (22.0)	199 (24.1)	201 (20.2)	
2009	304 (16.7)	136 (16.5)	168 (16.9)	
2010	338 (18.6)	158 (19.2)	180 (18.1)	
2011	367 (20.2)	169 (20.5)	198 (19.9)	
2012	225 (12.4)	87 (10.6)	138 (13.9)	
2013	110 (6.1)	47 (5.7)	63 (6.3)	
2014	76 (4.2)	29 (3.5)	47 (4.7)	
Age Group				0.004
21-24	552 (30.3)	238 (28.9)	314 (31.6)	
25-29	612 (33.6)	312 (37.8)	300 (30.2)	
30-34	431 (23.7)	188 (22.8)	243 (24.4)	
35-39	225 (12.4)	87 (10.6)	138 (13.9)	
Diagnosis Type				<0.001
CIN 2, 2/3	1313 (72.1)	516 (62.6)	797 (80.1)	
CIN 3, AIS ± CIN	507 (27.9)	309 (37.5)	198 (19.9)	
Race/Ethnicity				0.001
White	942 (51.8)	463 (56.1)	479 (48.1)	
Hispanic	326 (17.9)	148 (17.9)	178 (17.9)	
Black	256 (14.1)	94 (11.4)	162 (16.3)	
Other/Unknown	296 (16.3)	120 (14.6)	176 (17.7)	
Insurance				0.218
Private	1087 (59.7)	510 (61.8)	577 (58.0)	
Public/None	596 (32.8)	259 (31.24	337 (33.9)	
Other/Missing	137 (7.5)	56 (6.8)	81 (8.1)	
Area-based Measures				
Area race				0.076
<20% black	1297 (71.3)	605 (73.3)	692 (69.6)	
≥20% black	523 (28.7)	220 (26.7)	303 (30.5)	
Area ethnicity				0.631
<20% Hispanic	1247 (68.5)	570 (69.1)	677 (68.0)	
≥20% Hispanic	573 (31.5)	255 (30.9)	318 (32.0)	
Area poverty				0.702
<20% in poverty	1340 (73.6)	611 (74.1)	729 (73.3)	
≥20% poverty	480 (26.4)	214 (25.9)	266 (26.7)	

All data are presented as n (column %). Percentages may not sum to 100% due to rounding.
Abbreviations: AIS, adenocarcinoma in situ; CIN, cervical intraepithelial neoplasia.
[a] p-value is for χ^2 test

Figure 2. Trends in Prevalence of HPV 16/18 in CIN2+ Cases with High-Risk HPV Types During 2008-2014 in New Haven County, Connecticut, by Age Group

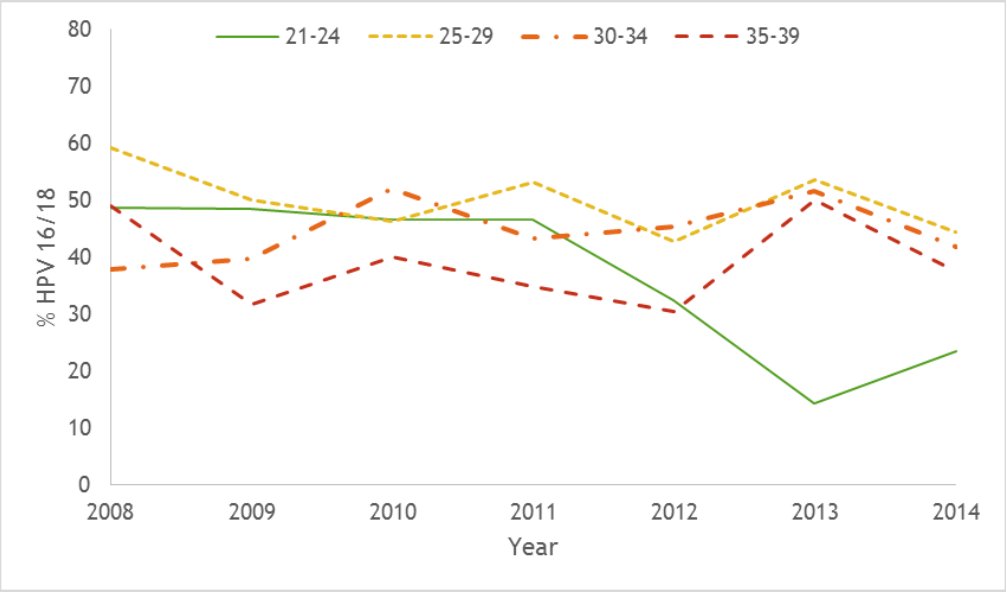

Table 2. Prevalence of HPV 16/18 in CIN2+ Cases with High-Risk HPV Types Among Women Aged 21-39 Years: Unadjusted Effects of Individual- and Area-Level Characteristics (n=1,820)

	Unadjusted Prevalence Ratio (95% CI)	p
Year		
2008	1.00	
2009	0.82 (0.61, 1.10)	0.187
2010	0.89 (0.67, 1.18)	0.416
2011	0.86 (0.65, 1.15)	0.306
2012	0.64 (0.46, 0.89)	0.008
2013	0.75 (0.49, 1.15)	0.193
2014	0.62 (0.38, 1.03)	0.065
Age Group		
21-24	1.20 (0.88, 1.65)	0.254
25-29	1.65 (1.21, 2.25)	0.002
30-34	1.23 (0.88, 1.71)	0.223
35-39	1.00	
Diagnosis Type		
CIN 2, 2/3	1.00	
CIN 3, AIS ± CIN	2.41 (1.95, 2.97)	<0.001
Race/Ethnicity		
White	1.00	
Hispanic	0.86 (0.67, 1.11)	0.243
Black	0.60 (0.45, 0.80)	<0.001
Other/Unknown	0.71 (0.54, 0.92)	0.010
Insurance		
Private	1.00	
Public/None	0.87 (0.71, 1.06)	0.173
Other/Missing	0.78 (0.55, 1.12)	0.182
Area-based Measures		
Area race		
<20% black	1.00	
≥20% black	0.83 (0.67, 1.03)	0.085
Area ethnicity		
<20% Hispanic	1.00	
≥20% Hispanic	0.95 (0.78, 1.17)	0.641
Area poverty		
<20% in poverty	1.00	
≥20% poverty	0.96 (0.77, 1.20)	0.716

Abbreviations: AIS, adenocarcinoma in situ; CIN, cervical intraepithelial neoplasia.

Table 3. Prevalence of HPV 16/18 in CIN2+ Cases with High-Risk HPV Types Among Women Aged 21-39 Years: Main Effect of Year, Adjusted for Age Group and Diagnosis (n=1,820)

	Adjusted Prevalence Ratio (95% CI)	p
Year		
2008	1.00	
2009	0.85 (0.62, 1.15)	0.285
2010	0.91 (0.68, 1.23)	0.548
2011	0.87 (0.65, 1.16)	0.346
2012	0.61 (0.43, 0.85)	0.004
2013	0.69 (0.44, 1.07)	0.097
2014	0.64 (0.39, 1.08)	0.093

Figure 3. Prevalence of HPV 16/18 in CIN2+ Cases with High-Risk HPV Types Among Women Aged 21-39 Years During 2008-2014, by Area-Based Race

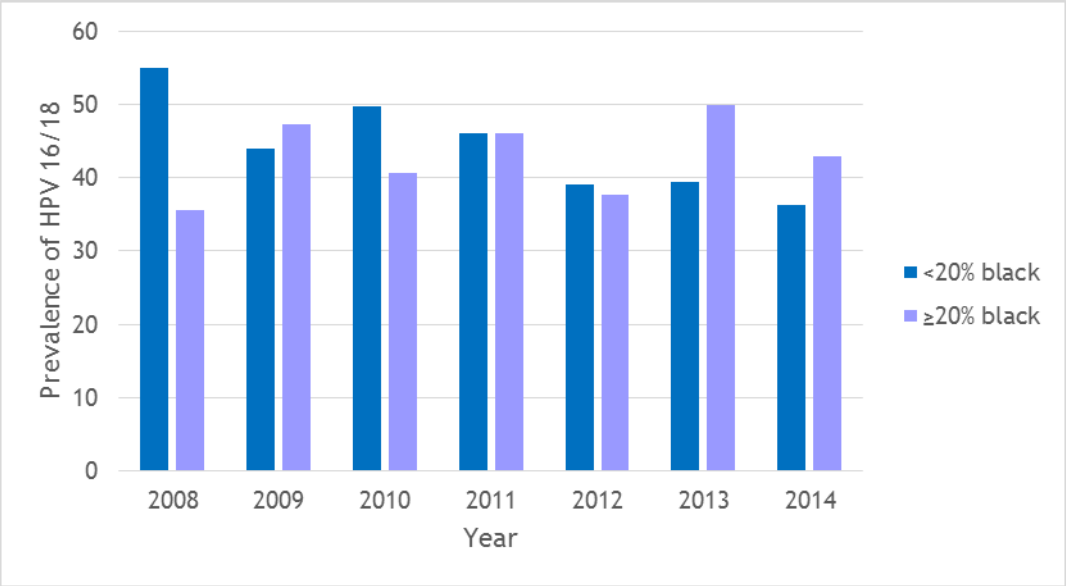

Table 4. Prevalence of HPV 16/18 in CIN2+ Cases with High-Risk HPV Types Among Women Aged 21-24 Years: Unadjusted Effects of Individual- and Area-Level Characteristics (n=522)

	Unadjusted Prevalence Ratio (95% CI)	p
Year		
2008-2009	1.00	
2010-2011	0.92 (0.63, 1.35)	0.685
2012-2014	0.39 (0.24, 0.63)	<0.001
Diagnosis Type		
CIN 2, 2/3	1.00	
CIN 3, AIS ± CIN	2.64 (1.74, 4.02)	<0.001
Race/Ethnicity		
White	1.00	
Hispanic	0.98 (0.61, 1.56)	0.933
Black	0.71 (0.44, 1.16)	0.172
Other/Unknown	1.09 (0.67, 1.78)	0.724
Insurance		
Private	1.00	
Public/None	1.19 (0.83, 1.72)	0.344
Other/Missing	0.93 (0.47, 1.81)	0.826
Area-based Measures		
Area race		
<20% black	1.00	
≥20% black	1.02 (0.71, 1.47)	0.895
Area ethnicity		
<20% Hispanic	1.00	
≥20% Hispanic	1.42 (1.01, 2.00)	0.045
Area poverty		
<20% in poverty	1.00	
≥20% poverty	1.40 (0.98, 2.01)	0.066

Abbreviations: AIS, adenocarcinoma in situ; CIN, cervical intraepithelial neoplasia.

Table 5. Prevalence of HPV 16/18 in CIN2+ Cases with High-Risk HPV Types Among Women Aged 21-24 Years: Main Effect of Year, Adjusted for Diagnosis (n=522)

	Adjusted Prevalence Ratio (95% CI)	p
Years		
2008-2009	1.00	
2010-2011	0.87 (0.59, 1.28)	0.468
2012-2014	0.39 (0.40, 0.63)	<0.001

Figure 4. Prevalence of HPV 16/18 in CIN2+ Cases with High-Risk HPV Types Among Women Aged 21-24 Years During 2008-2014, by Area-Based Measures of Race (Panel A), Ethnicity (Panel B), and Poverty (Panel C)